

REMARKS

Claims 1, 2, 4-10, 13-19 are pending and have been rejected. Claims 3, 11-12, and 20-60 have been canceled. Claim 16 has been amended due to a typographical error, without prejudice.

I. Double Patenting

The Examiner has rejected Claims 1, 2, 4-10, and 13-19 on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,765,001.

The Examiner indicates that the terminal disclaimer filed on November 16, 2007, is currently under review and the rejection will be withdrawn once the terminal disclaimer is found proper. See Office Action, p. 6.

II. 35 U.S.C. § 103(a)

Before addressing the rejections raised by the Examiner, a few preliminary comments concerning the claimed subject matter may be helpful.

The claimed invention is a composition for delivering corticosteroids. The claimed composition has penetration enhancers (p), solvents (s) and emulsifiers (e). According to the claims, these three components are present in a ratio of $p/(p+s+e)$, such that this ratio (also referred to as the "PE Ratio") is at least about 0.90. It is important to note that the claims do not concern themselves with the absolute amounts of any of these ingredients in the overall composition. Similarly, the claims do not concern themselves with the proportion of any of these ingredients in the overall composition. Instead, the claims deal with the ratio of the ingredients to each other, a relationship that is stated as the $p/(p+s+e)$ ratio.

This feature of the claims has been overlooked by the Examiner, and this led to an error which fatally infects all of the current rejections.

Instead of addressing the $p/(p+s+e)$ ratio which is and has always been a feature of the claims, the Examiner has focused on the amounts of the separate ingredients. Even when this ratio has been called to the Examiner's attention, it clearly has not been appreciated. Thus, the Examiner has dismissed the feature of the claims by saying, "[M]ore penetration enhancer, more penetration. Is that obvious?" It is submitted that this statement reveals the fundamental misunderstanding that underlies all of the rejections under § 103. The claimed invention is not using more penetration enhancer to get more penetration. In fact, the required ratio of $p/(p+s+e)$ can be achieved (or lost) without ever changing the amount of penetration enhancer in the composition. Compositions can achieve (or lose) the required ratio by varying the amount of solvents (s) and emulsifiers (e), while holding the amount of penetration enhancer (p) constant. Clearly, the claimed invention is not "more penetration enhancer, more penetration." Yet this is the basis for the rejections under § 103.

This error is found elsewhere in the current Office Action. Immediately before the above quoted remark, the Examiner argues:

Applicants remarks as to the PE Ratio ... are not persuasive. One of ordinary skill in the art would have recognized that the concentration of the penetration enhancer would be a result effective parameter and optimization of such parameter would have been within the purview of an ordinary skilled artisan. (emphasis added)

Again the Examiner's remarks reveal a fundamental misunderstanding of the claims. The claimed invention is not based on the concentration of the penetration enhancer in the composition. As was pointed out earlier in this response, the concentration of the penetration

enhancer can be held constant while solvents and emulsifiers varied to produce compositions that achieve (or fail to achieve) the ratio called for by the claims. The current Office Action simply fails to appreciate this important feature of the claimed invention.

This error infects the way in which the Examiner applies the cited references in the specific rejections. The Applicant will discuss this below in the context of each reference and rejection.

A. Claims 1, 2, 4-10, and 13-19 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Poulsen (US 3,934,013).

Applicant respectfully traverses this rejection. The Examiner fails to establish a *prima facie* case of obviousness based on Poulsen with regard to the present invention. To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest *all* of the claim limitations. MPEP §2142; *Velandar v. Garner*, 348 F.3d 1359, 1363 (Fed. Cir. 2003).

Applicant agrees with the Examiner that Poulsen “does not teach some of the particular percentages of corticosteroid or propylene glycol herein.” *See* Office Action mailed February 26, 2008, p. 3. But this is only the beginning of Poulsen’s shortcomings. In addition to not teaching or suggesting the particular percentages of corticosteroid or propylene glycol, Poulsen also does not teach or suggest the ratio of ingredients, that is called for by the claims.

The Examiner is also mistaken in asserting that “the fatty alcohol or ester is considered as [sic] to meet the limitation of penetration enhancer since it is well known that fatty compound would enhance the penetration of topical therapeutic compounds. *See*, e.g., page 2, third paragraph in the specification.” *See* Office Action mailed February 26, 2008, p. 3. However, the

Examiner's assertion is misplaced and misinterprets the meaning of page 2, third paragraph of the present specification. Poulsen states that "[s]uitable fatty alcohols include cetyl alcohol, stearyl alcohol, behenyl alcohol and the like." Col. 10, lines 47-49. The fatty alcohols described in Poulsen are not penetration enhancers. Rather, the fatty alcohols disclosed are known to be non-solvent/emulsifiers. *See* ¶ 0033. Further, as described in the instant specification at paragraph 34, stearyl alcohol is defined as a non-solvent/emulsifier not a penetration enhancer. Additionally, cetyl alcohol and behenyl alcohol are not penetration enhancers.

Poulsen also does not teach or suggest a ratio of penetration enhancers to penetration enhancers and solvents and emulsifiers ("PE Ratio") of at least about 0.90. Poulsen does not teach or suggest (or even recognize) this novel and critical ratio, or that the specific PE Ratios correlate to particular vasoconstrictor scores. This result effective parameter (the PE Ratio) is described for the first time in this application.

Since Poulsen is also silent about the two or more penetration enhancers, the PE Ratio, and a PE Ratio of at least about 0.90, one of ordinary skill in the art would not have been motivated to employ the corticosteroid(s) and penetration enhancers of the present invention, much less in the amounts necessary to achieve a PE Ratio of at least about 0.90. Further, for optimization of a particular Result-Effective Variable (such as the PE Ratio) to be considered obvious, the particular variable must first be recognized, which is not the case with the prior art of record. MPEP §2144.05. Poulsen's silence regarding particular elements of the claimed invention cannot and does not lend itself to mere optimization and thus, the claimed invention is not obvious over the prior art.

Therefore, based upon the fact that the cited reference fails to teach or suggest each and every claim element, the claims are not obvious over Poulsen. Applicant respectfully submits that this prima facie case has not been established and the rejection should be removed.

i.) Unexpected Results.

Applicant submitted the Gans Declaration as evidence of the unexpected results, including the increased vasoconstrictor scoring and class of steroid. The Examiner rejected the unexpected results evidence as “insufficient” because “It refer(s) only to the system described in the above-referenced application and not to the individual claims of the application. Particularly, as shown in the specification, it [is] only limited to the particular glucocorticoid with particular penetration enhancers.” The Examiner goes on to state that the showing is “not commensurate in scope with the claims.” The Examiner’s position violates MPEP §716.02(c)I which provides that, “an exemplary showing may be sufficient to establish a reasonable correlation between the showing and the entire scope of the claim, when viewed by a skilled artisan.” See In re Chupp, 816 F.2d 643, 646 (Fed. Cir. 1987). The Gans declaration is such an exemplary showing, which would be recognized by a skilled artisan.

Further, “if the evidence is deemed insufficient to rebut the prima facie case of obviousness, Office personnel should specifically set forth the facts and reasoning that justify this conclusion.” While Applicant fully believes the prima facie case of obviousness has not been established, assuming *arguendo* it has and has not been overcome, if the Examiner still disagrees that the unexpected results are sufficient, he is required to set forth his facts and reasoning.

B. Claims 1, 2, 4-10, and 13-19 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Poulsen in view of Bennett.

Applicant respectfully traverses this rejection. The Examiner fails to establish a *prima facie* case of obviousness based on Poulsen in view of Bennett with regard to the present invention.

As discussed above, Poulsen fails to teach or suggest the claim elements of two or more penetration enhancers and a PE Ratio of at least about 0.90 and above or that particular PE Ratio values correlate with particular vasoconstrictor scores. Bennett does not make up for these deficiencies and also fails to teach or suggest the claimed invention on its own.

The Examiner's reading of Bennett shares many of the same flaws as his reading of Poulsen. Bennett does not recognize the existence of the PE Ratio much less suggest that it is a result effective variable, or (if it is a result effective variable) how it can be manipulated to achieve any particular result. For optimization of a particular Result-Effective Variable (such as the PE Ratio) to be considered obvious, the particular variable must first be recognized, which is not the case with the prior art of record. MPEP §2144.05. Additionally, Bennett fails to teach or suggest that such a ratio correlates between improved potency and unexpectedly high vasoconstrictor scores. In fact, none of the taught compositions have the claimed PE Ratio of at least about 0.90.

Therefore, based upon the fact that the cited references fail to teach or suggest each and every claim element, the claims are not obvious over Poulsen in view of Bennett. Applicant respectfully submits that the *prima facie* case of obviousness has not been established and the rejection should be removed.

C. Claims 8-9 have been rejected under 35 U.S.C. §103(a) as being “unpatentable over Poulsen as applied to claims 1-7 and 10, 13-19 above, and further in view of the PDR entries of Lidex-Synalar.”

As discussed above, Poulsen fails to teach or suggest the elements of two or more penetration enhancers and a PE Ratio of at least about 0.90 or that particular PE Ratio values correlate with particular vasoconstrictor scores. The PDR reference when combined with Poulsen does not make up for the elements missing from Poulsen.

Once again the Examiner’s error in understanding the claims infects his reading of another reference – the PDR entry for Lidex-Synalar (referred to as “Lidex”). The PDR entry does not recognize the existence of the ration of $p/(p+s+e)$ – the PE Ratio. Indeed, even with the hindsight teachings of the applicant’s own disclosures, it is impossible to calculate the PE Ratio of the Lidex® product from its PDR entry. How can a reference which is unaware of the existence of the PE Ratio and doesn’t have enough information to calculate a PE Ration render the claimed invention obvious? The PDR’s disclosure cannot make one skilled in the art aware of this ratio, cannot suggest that it is a result effective variable, and cannot suggest that it be controlled (that is kept about 0.90) to achieve a particular result. Far from supplementing Poulsen, the PDR shares fully in all of Poulsen’s shortcomings.

Moreover, the PDR reference is for Lidex®, which is a Class II steroid. *See* Table II, Specification, p. 11. In contrast, the present invention shows the unexpected ability to produce vasoconstrictor scores for Class I drugs using the components of the present invention in the specified PE Ratio. Specification, p. 11, paragraph 27.

Therefore, Poulsen, the PDR reference, nor the combination of references teach or suggest all of the claim elements and there is no teaching or suggestion to combine the references.

Therefore, based upon the fact that the cited references fail to teach or suggest each and every claim element, the claims are not obvious over Poulsen or in further view of the PDR entries of Lidex. Applicant respectfully submits that no prima facie case of obviousness has been established, and this rejection should be removed. Alternatively, assuming *arguendo* a prima facie case exists, unexpected results exist and this rejection should be removed.

CONCLUSION

In view of the foregoing remarks, Applicant respectfully requests consideration and allowance of the pending claims. Finally, Applicant respectfully submits a request for a personal interview with the Examiner, in order to further resolve any outstanding issues.

Authorization of Deposit Account

The Commissioner is hereby authorized to charge any fees which may be required during the entire pendency of this application, or credit any overpayment, to Deposit Account No. 18-0586. This authorization also hereby includes a request for any extensions of time of the appropriate length required upon the filing of any reply during the entire pendency of this application.

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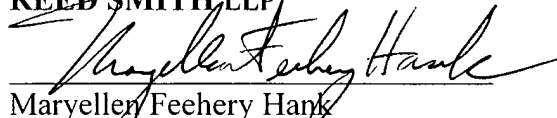
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